CLAIMS

1. A method for relieving acute or chronic pain comprising:

administering to a subject in need thereof an effective amount of an agent which inhibits expression of PSD93 or PSD95, whereby acute or chronic pain experienced by the subject is relieved.

2. The method of claim 1 wherein the agent is an antisense oligonucleotide which is complementary to mRNA encoding PSD93.
3. The method of claim 1 wherein the agent is an antisense oligonucleotide which is complementary to mRNA encoding PSD95.
4. The method of claim 1 wherein the antisense oligonucleotide is complementary to nucleotides encoding a PDZ domain.
5. The method of claim 3 wherein the antisense oligonucleotide is complementary to nucleotides 241 to 258.
6. The method of claim 1 wherein the agent is administered intrathecally.
7. A method for treating or preventing hyperalgesia comprising:

administering to a subject in need thereof an effective amount of an agent which inhibits expression of PSD93 or PSD95, whereby hyperalgesia experienced by the subject is relieved.

8. The method of claim 7 wherein the agent is an antisense oligonucleotide which is complementary to mRNA encoding PSD93.
9. The method of claim 7 wherein the agent is an antisense oligonucleotide which is complementary to mRNA encoding PSD95.
10. The method of claim 7 wherein the antisense oligonucleotide is complementary to nucleotides encoding a PDZ domain.
11. The method of claim 9 wherein the antisense oligonucleotide is complementary to nucleotides 241 to 258.
12. The method of claim 7 wherein the agent is administered intrathecally.
13. A method of reducing a threshold for anesthesia comprising:

administering to a subject an anesthetic and an agent which inhibits expression of PSD93 or PSD95, wherein the amount of anesthetic administered is less than the amount required in the absence of the agent to achieve a desired anesthetic effect, whereby the desired anesthetic effect is achieved.

14. The method of claim 13 wherein the agent is an antisense oligonucleotide which is complementary to mRNA encoding PSD93.
15. The method of claim 13 wherein the agent is an antisense oligonucleotide which is complementary to mRNA encoding PSD95.
16. The method of claim 13 wherein the antisense oligonucleotide is complementary to nucleotides encoding a PDZ domain.
17. The method of claim 15 wherein the antisense oligonucleotide is complementary to nucleotides 241 to 258.
18. The method of claim 13 wherein the agent is administered intrathecally.
19. A pharmaceutical formulation comprising an isolated and purified antisense polynucleotide which is complementary to PSD95 or PSD93 mRNA.
20. The pharmaceutical formulation of claim 19 wherein the polynucleotide is complementary to nucleotides encoding a PDZ domain.
21. The pharmaceutical formulation of claim 19 wherein the polynucleotide is complementary to nucleotides encoding a C-terminal PDZ domain.
22. The pharmaceutical formulation of claim 19 wherein the polynucleotide is complementary to nucleotides 241 to 258 of PSD95.
23. The pharmaceutical formulation of claim 19 wherein the polynucleotide is complementary to PSD93 mRNA.
24. The pharmaceutical formulation of claim 19 wherein the polynucleotide is manufactured under regulatory-approved conditions for administration to humans.
25. The pharmaceutical formulation of claim 19 wherein the polynucleotide is pyrogen-free.
26. A method for relieving acute or chronic pain comprising:

administering to a subject in need thereof an effective amount of an agent which inhibits interaction of a first protein selected from the group consisting of PSD93 and PSD95, with a second protein selected from the group consisting of nNOS and NMDA receptor, wherein the agent does not cause cardiovascular or respiratory depression, whereby acute or chronic pain experienced by the subject is relieved.

27. The method of claim 26 wherein the agent is administered intrathecally.
28. A method for treating or preventing hyperalgesia comprising:

administering to a subject in need thereof an effective amount of an agent which inhibits interaction of a first protein selected from the group consisting of PSD93 and

PSD95, with a second protein selected from the group consisting of nNOS and NMDA receptor, wherein the agent does not cause cardiovascular or respiratory depression, whereby hyperalgesia experienced by the subject is relieved.

29. The method of claim 28 wherein the agent is administered intrathecally.

30. A method of reducing a threshold for anesthesia comprising:

administering to a subject an anesthetic and an agent which inhibits interaction of a first protein selected from the group consisting of PSD93 and PSD95, with a second protein selected from the group consisting of nNOS and NMDA receptor, wherein the agent does not cause cardiovascular or respiratory depression, wherein the amount of anesthetic administered is less than the amount required in the absence of the agent to achieve a desired anesthetic effect, whereby the desired anesthetic effect is achieved.

31. The method of claim 30 wherein the agent is administered intrathecally.

32. The method of claim 26, 28, or 30 wherein the agent binds to a PDZ domain of the first or second protein.

33. The method of claim 26, 28, or 30 wherein the agent does not impair motor function.

34. The method of claim 13 or 30 wherein the anesthetic is selected from the group consisting of halothane, isoflurane, desflurane, xenon, and sevoflurane.

35. A method of anesthetizing a subject comprising:

administering to a subject an agent which inhibits expression of PSD93 or PSD95, whereby the agent renders the subject unconscious or sedated.

36. The method of claim 35 wherein the agent is an antisense oligonucleotide which is complementary to mRNA encoding PSD93.

37. The method of claim 35 wherein the agent is an antisense oligonucleotide which is complementary to mRNA encoding PSD95.

38. The method of claim 35 wherein the antisense oligonucleotide is complementary to nucleotides encoding a PDZ domain.

39. The method of claim 37 wherein the antisense oligonucleotide is complementary to nucleotides 241 to 258.

40. The method of claim 35 wherein the agent is adminstered intrathecally.

41. A method of anesthetizing a subject comprising:

administering to a subject an agent which inhibits interaction of a first protein selected from the group consisting of PSD93 and PSD95, with a second protein selected from the group consisting of nNOS and NMDA receptor, wherein the agent does not cause cardiovascular or respiratory depression, whereby the agent renders the subject unconscious or sedated.

42. The method of claim 41 wherein the agent is administered intrathecally.

43. The method of claim 41 wherein the agent binds to a PDZ domain of the first or second protein.

44. The method of claim 41 wherein the agent does not impair motor function.

45. A method of screening for substances useful for relieving pain or inducing unconsciousness or sedation, comprising:

contacting a test substance with a first protein and a second protein under conditions where the first protein and the second protein bind to each other, wherein the first protein is selected from the group consisting of PSD93, PSD95, and a combination thereof, wherein the second protein is selected from the group consisting of nNOS, NMDA receptor, NR2A subunit, NR2B subunit, and combinations thereof;

determining an amount selected from the group consisting of: free nNOS, free PSD93, free PSD95, free NMDA receptor, free NR2A subunit, free NR2B subunit, bound nNOS, bound PSD93, bound PSD95, bound NMDA receptor, bound NR2A subunit, bound NR2B subunit and combinations thereof;

identifying a test substance which increases the amount of free nNOS, free PSD93, free PSD95, free NMDA receptor, free NR2A subunit, or free NR2B subunit, or which decreases the amount of bound nNOS, bound PSD93, bound PSD95, bound NMDA receptor, bound NR2A subunit, or bound NR2B subunit as a candidate drug for relieving pain or inducing unconsciousness or sedation.

46. The method of claim 45 wherein the step of contacting is done *in vitro*.

47. The method of claim 45 wherein the step of contacting is done in yeast cells containing recombinant forms of the first and second proteins.

48. The method of claim 47 wherein the first and second recombinant proteins are each fused to a first and second yeast protein, wherein the first and second yeast proteins reconstitute a functional transcriptional activator when brought into physical proximity by binding of the first recombinant protein to the second recombinant protein.

49. The method of claim 45 further comprising the step of:

testing an identified candidate drug in an animal to determine if the candidate drug relieves pain or induces unconsciousness or sedation.

50. The method of claim 45 wherein the test substance is contacted with PSD95 and nNOS.

51. The method of claim 45 wherein the test substance is contacted with PSD95 and NMDA receptor.

52. The method of claim 45 wherein the test substance is contacted with PSD95, nNOS, and NMDA receptor.

53. The method of claim 45 wherein the test substance is contacted with PSD95 and NR2A.

54. The method of claim 45 wherein the test substance is contacted with PSD95 and NR2B.

55. The method of claim 45 wherein the test substance is contacted with PSD93 and nNOS.

56. The method of claim 45 wherein the test substance is contacted with PSD93 and NMDA receptor.

57. The method of claim 45 wherein the test substance is contacted with PSD93, nNOS, and NMDA receptor.

58. The method of claim 45 wherein the test substance is contacted with PSD93 and NR2A.

59. The method of claim 45 wherein the test substance is contacted with PSD93 and NR2B.

60. The method of claim 45 wherein surface plasmon resonance is used to determine said amount.

61. The method of claim 45 wherein antibodies are used to determine said amount.

62. The method of claim 13 wherein the anesthetic is an inhalational anesthetic.

63. The method of claim 30 wherein the anesthetic is an inhalational anesthetic.

64. The method of claim 13 wherein the anesthetic is selected from the group consisting of urethane, chloral hydrate, and sodium pentobarbitone.

65. The method of claim 30 wherein the anesthetic is selected from the group consisting of urethane, chloral hydrate, and sodium pentobarbitone.